SURVEILLANCE REPORT

Annual Epidemiological Report for 2016

Invasive pneumococcal disease

Key facts

- In 2016, 21 986 confirmed cases of invasive pneumococcal disease (IPD) were reported in the EU/EEA.
- The notification rate was 5.4 cases per 100 000 population, similar to rates observed in previous years.
- Age-specific rates were highest in those aged 65 years and over (15.8 cases per 100 000 population), followed by infants under one year of age (11.9 cases per 100 000 population).
- The 10 most common serotypes were 8, 3, 12F, 22F, 19A, 9N, 15A, 10A, 33F and 11A (in order of frequency), accounting for 64% of typed isolates.
- Of all cases under five years of age, 71% were caused by a serotype not included in any pneumococcal conjugate vaccine (PCV).
- Among cases aged 65 years and over, 74% were caused by a PPV23 serotype and 30% were caused by a PCV13 serotype.

Methods

This report is based on data for 2016 retrieved from The European Surveillance System (TESSy) on 15 March 2018. TESSy is a system for the collection, analysis and dissemination of data on communicable diseases. EU Member States and EEA countries contribute to the system by uploading infectious disease surveillance data at regular intervals.

For a detailed description of methods used to produce this report, please refer to the *Methods* chapter [1].

An overview of the national surveillance systems is available online [2].

Additional data on this disease are accessible from ECDC's online *Surveillance atlas of infectious diseases* [3].

In 2016, 29 Member States reported data on invasive pneumococcal disease (IPD). Twenty-four Member States used the EU-2008/2012 case definition. One Member State used the EU-2002 case definition and four Member States used alternative case definitions. The EU-2008/2012 case definition differs from the EU-2002 case definition by not including possible and probable cases and including detection of *S. pneumoniae* antigens at a normally sterile site as a confirmed case [4].

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Stockholm, August 2018

National IPD surveillance systems are heterogeneous. Of the 29 countries reporting data, 22 countries conduct surveillance with compulsory reporting and national coverage. Four countries perform surveillance through voluntary sentinel systems. France, the Netherlands and Spain have surveillance systems that cover 100%, 25% and 80% of the national population respectively. The population coverage of Belgium's surveillance system is unknown, therefore notification rates were not calculated.

IPD data from France are reported through two different systems: one relying on reports from physicians (FR-EPIBAC) and the other based on laboratories (FR-PNEUMO-NRL). Data reported from FR-PNEUMO-NRL are used for the analysis of serotype and antimicrobial susceptibility, while data reported from FR-EPIBAC provide epidemiological and clinical information for analysis. Germany has a voluntary laboratory-based surveillance system and does not report data to ECDC [5]. All countries except Belgium, Bulgaria and Croatia reported case-based data [2].

Epidemiology

In 2016, 21 986 confirmed cases of IPD were reported by 29 countries. The notification rate was 5.4 cases per 100 000 population, which was similar to rates observed in most previous years (Table 1). The United Kingdom had the highest number of confirmed cases, followed by France. The highest notification rates were reported in Finland, the Netherlands, Sweden and Slovenia (Table 1, Figure 1).

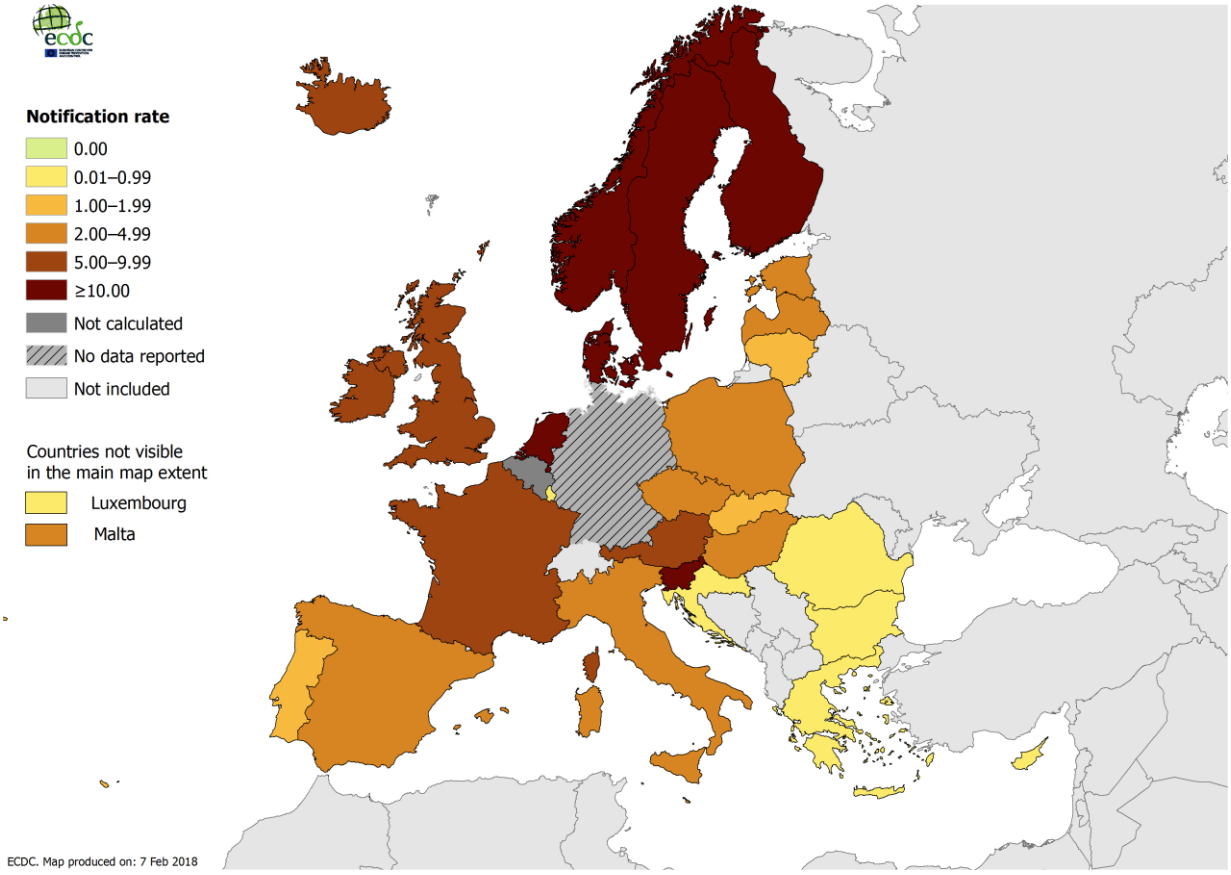
Table 1. Distribution of confirmed cases of invasive pneumococcal disease by country and year, EU/EEA, 2012–2016

Country	2012		2013		2014		2015		2016			
	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Confirmed cases	Rate	ASR	Reported cases
Austria	234	2.8	350	4.1	322	3.8	422	4.9	439	5.1	4.8	439
Belgium	1 738	-	1 604	-	1 192	-	1 362	-	1 329	-	-	1 329
Bulgaria	19	0.3	17	0.2	21	0.3	31	0.4	35	0.5	0.5	35
Croatia	18	0.4	16	0.4	27	0.6	24	0.6	14	0.3	-	14
Cyprus	19	2.2	8	0.9	14	1.6	9	1.1	5	0.6	0.7	5
Czech Republic	335	3.2	424	4.0	337	3.2	413	3.9	323	3.1	2.9	323
Denmark	882	15.8	842	15.0	725	12.9	807	14.3	731	12.8	12.2	731
Estonia	20	1.5	24	1.8	12	0.9	24	1.8	30	2.3	2.2	30
Finland	752	13.9	724	13.3	703	12.9	815	14.9	817	14.9	13.9	817
France	4 430	9.2	3 687	7.8	3 184	6.6	3 299	6.8	3 800	5.7	5.5	3 800
Germany												
Greece	43	0.4	40	0.4	30	0.3	55	0.5	52	0.5	0.4	52
Hungary	186	1.9	202	2.0	150	1.5	189	1.9	226	2.3	2.2	226
Iceland	27	8.4	19	5.9	24	7.4	25	7.6	19	5.7	6.2	19
Ireland	350	7.6	347	7.6	342	7.4	370	8.0	378	8.0	9.2	378
Italy	814	1.4	977	1.6	957	1.6	1 248	2.1	1 529	2.5	2.2	1 529
Latvia	56	2.7	56	2.8	51	2.5	87	4.4	65	3.3	3.0	65
Liechtenstein												
Lithuania	7	0.2	17	0.6	6	0.2	25	0.9	56	1.9	1.8	56
Luxembourg	1	0.2	1	0.2	1	0.2	0	0.0	1	0.2	0.2	1
Malta	15	3.6	6	1.4	22	5.2	9	2.1	11	2.5	2.4	11
Netherlands	635	15.2	652	15.5	546	13.0	667	15.8	631	14.9	14.3	636
Norway	626	12.6	620	12.3	69	11.1	522	10.1	599	11.5	12.0	599
Poland	441	1.2	540	1.4	705	1.9	979	2.6	962	2.5	2.6	962
Portugal							142	1.4	163	1.6	1.5	163
Romania	79	0.4	92	0.5	62	0.3	53	0.3	50	0.3	0.3	50
Slovakia	49	0.9	84	1.6	78	1.4	68	1.3	59	1.1	1.1	59
Slovenia	245	11.9	278	13.5	276	13.4	332	16.1	281	13.6	13.0	281
Spain	2260	6.0	2026	5.4	1 856	5.0	2037	5.5	1 825	4.9	4.6	1 825
Sweden	1387	14.6	1316	13.8	1 159	12.0	1314	13.5	1 351	13.7	12.8	1 351
United Kingdom	5 208	8.2	5 045	7.9	4 157	6.5	5 796	8.9	6 205	9.5	9.4	6 205
EU/EEA	**20 876**	**5.7**	**20 014**	**5.5**	**17 528**	**4.8**	**21 124**	**5.6**	**21 986**	**5.4**	**5.2**	**21 991**

Source: Country reports; ASR: Age-standardised rate; : No data reported; -: No notification rate calculated.

Note: National coverage in France is calculated based on the entire French population. However, the surveillance system only collects data from metropolitan France, thus the coverage of the surveillance system shown here for France is underestimated. The number of cases presented from France was collected through the FR-EPIBAC surveillance system.

Figure 1. Rates of confirmed cases of invasive pneumococcal disease per 100 000 population by country, EU/EEA, 2016

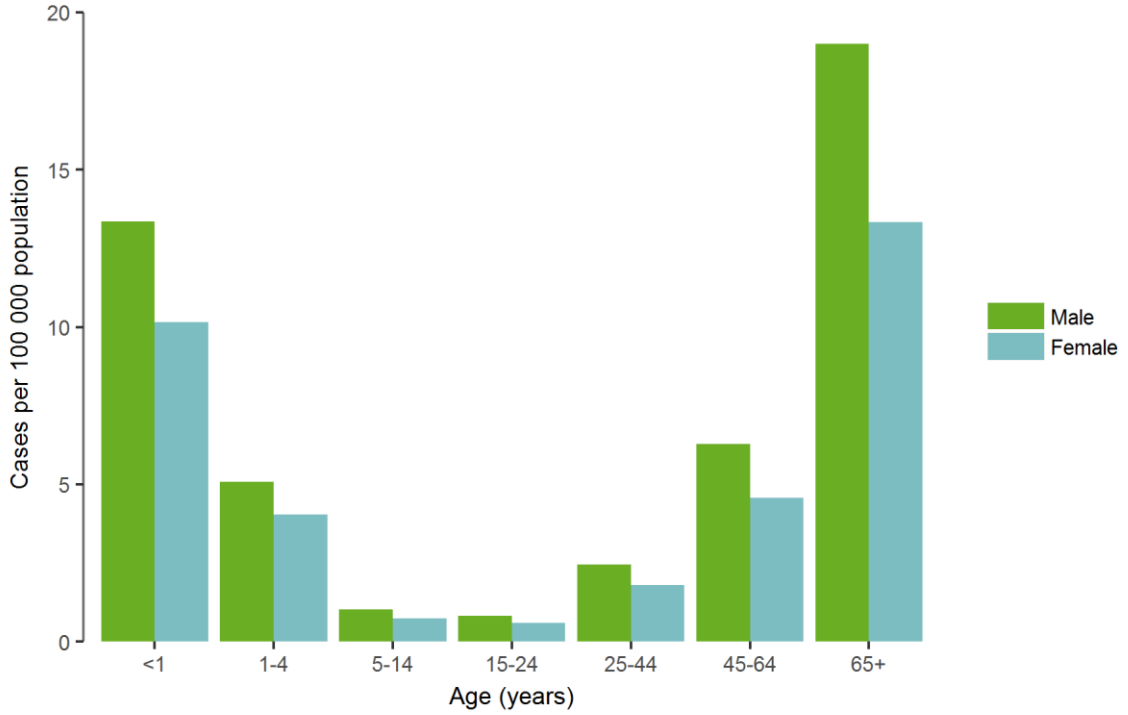


Source: Country reports from Austria, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

Age and gender distribution

In 2016, IPD was predominantly reported in the elderly and in infants, with 15.8 confirmed cases per 100 000 population in adults aged 65 years or older and 11.9 confirmed cases per 100 000 population in children under one year of age (Figure 2). As in previous years, the rates of disease were lowest in persons between 5 and 44 years of age. There was a predominance of cases in males in all age groups, resulting in an overall male-to-female ratio of 1.2:1.

Figure 2. Rate per 100 000 population of confirmed cases of invasive pneumococcal disease by age and gender, EU/EEA, 2016

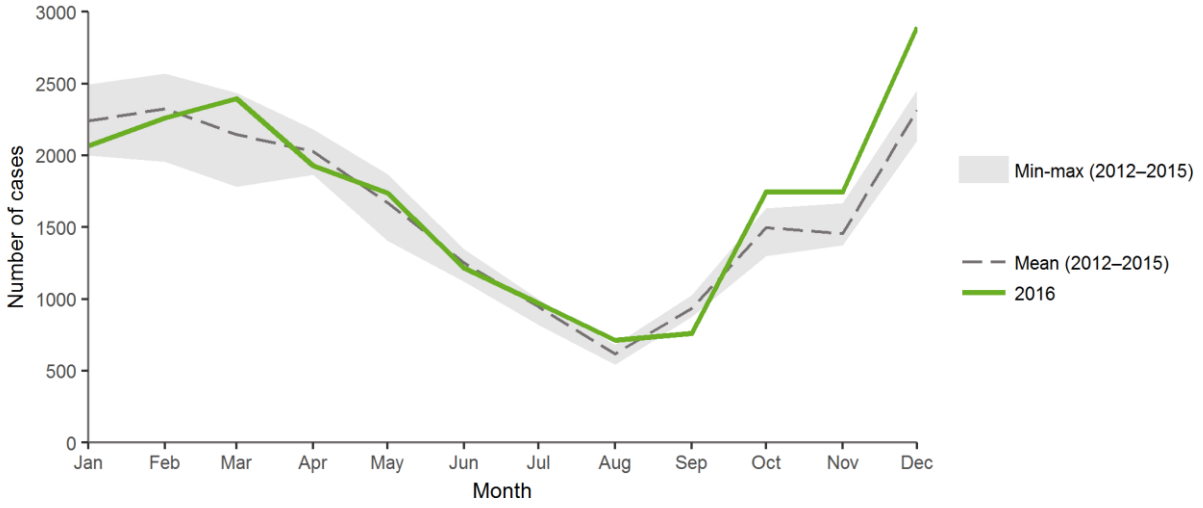


Source: Country reports from Austria, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

Seasonality and trend

The seasonal distribution of IPD cases followed a pattern similar to other respiratory diseases. Case numbers were lowest during the summer and increased rapidly with the onset of autumn and winter, peaking in March and December (Figure 3). A similar pattern was observed from 2012 to 2015, although the number of cases in the last three months of 2016 was higher than in previous years. IPD notification rates remained fairly stable over the same period, with the lowest value reported in 2014 (Table 1).

Figure 3. Distribution of confirmed invasive pneumococcal disease cases by month, EU/EEA, 2016 and 2012–2015



Source: Country reports from Austria, Belgium, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

Serotype

Different serotypes are covered by the pneumococcal vaccines:

- 7-valent pneumococcal conjugate vaccine (PCV7): 4, 6B, 9V, 14, 18C, 19F, 23F
- 10-valent PCV (PCV10): 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F
- 13-valent PCV (PCV13): 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F, 3, 6A, 19A. Although serotype 6A is included in PCV13 and not in PCV7, it is considered to be a PCV7 serotype in the analysis due to documented cross-protection provided by the serotype 6B antigen in PCV7.
- 23-valent pneumococcal polysaccharide vaccine (PPV23): 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F.

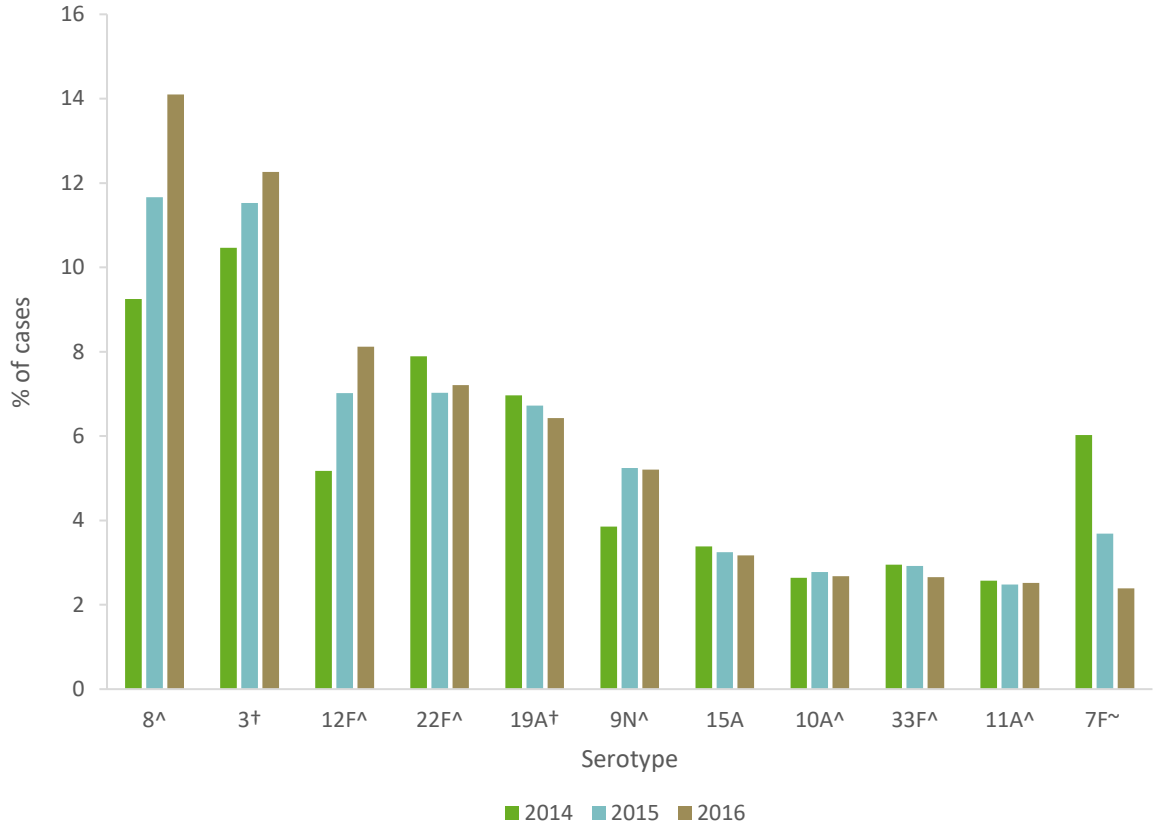
Data on serotype were reported for 15 918 (72%) of 21 986 cases in 24 EU/EEA countries for 2016. The 10 most common serotypes were 8, 3, 12F, 22F, 19A, 9N, 15A, 10A, 33F and 11A (ordered by frequency), accounting for 64% of all cases with known serotype. An increase in the frequency of the three most frequent serotypes was observed among countries reporting throughout the period 2014-2016: serotype 12F increased by 57%, 8 by 52% and 3 by 17%. During the same period, the frequency of 7F decreased by 60% (Figure 4).

Among cases under one year of age, serotype 8 was the most common, followed by 3. For children aged 1–4 years, serotypes 19A, 3 and 12F were the most common (Table 2). Of all cases aged under five years in 2016, 10% were caused by a PCV7 serotype (4, 6A, 6B, 9V, 14, 18C, 19F, 23F), 2% by a PCV10non7 serotype (1, 5, 7F) and 16% by a PCV13non10 serotype (3, 19A). The proportion of cases caused by PCV10non7 and PCV7 serotypes has decreased since 2013. In 2016, 71% of cases under five years of age were caused by a serotype not included in any PCV, an increase from 60% in 2013 (Figure 5).

Among cases aged 5–64 years old, 9% were caused by a PCV7 serotype, 5% by a PCV10non7 serotype, and 18% by a PCV13non10 serotype. The proportion of cases caused by PCV7 and PCV10non7 serotypes has decreased since 2013 (13% and 19% respectively). The proportion of cases caused by non-PCV serotypes has increased from 52% in 2013 to 69% in 2016.

Among adults 65 years and over, the most frequent serotypes were 3 and 8 (Table 2). Seventy-four percent were caused by a PPV23 serotype and 30% were caused by a PCV13 serotype. The proportion caused by a PCV13 serotype has declined since 2013 (40%). The proportion of cases among adults ≥ 65 years old caused by a PPV23 serotype has remained between 72% and 74% over 2013-2016. Twenty-six percent of cases aged 65 years old and over were caused by a serotype neither covered by PCV13 nor PPV23 in 2016, a slight decrease compared with previous years (Figure 6).

Figure 4. Distribution of confirmed cases of invasive pneumococcal disease: most common *S. pneumoniae* serotypes in 2014 (n=11 782), 2015 (n=15 403) and 2016 (n=15 905)



~ Covered by PCV10, PCV13 and PPV23
† Covered by PCV13 and PPV23
^ Covered by PPV23

Source: Country reports from Austria, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

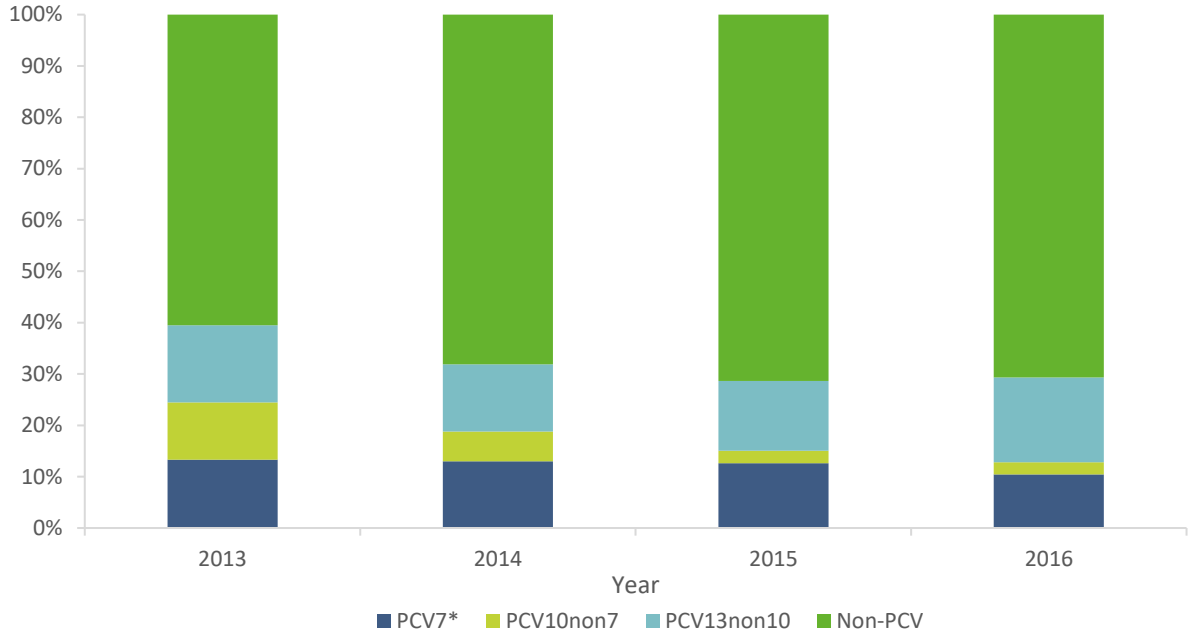
Table 2. Proportion of the five most frequent serotypes of *S. pneumoniae* from confirmed cases of invasive pneumococcal disease by age group, 2016 (n=15 887*)

Age group (years)	<1	1–4	5–14	15–24	25–44	45–64	≥65
Five most common serotypes by age group (% of all cases per age group)	8 (12.1%)	19A (10.0%)	8 (9.4%)	8 (24.6%)	8 (18.8%)	8 (16.3%)	3 (13.3%)
	3 (9.2%)	12F (7.7%)	3 (8.7%)	12F (12.3%)	12F (13.0%)	3 (12.8%)	8 (12.7%)
	10A (6.9%)	3 (7.7%)	19A (7.0%)	3 (7.4%)	3 (9.9%)	12F (10.4%)	22F (8.2%)
	12F (6.7%)	24F (7.1%)	12F (6.6%)	7F (7.0%)	19A (6.0%)	22F (6.7%)	19A (6.5%)
	24F (6.4%)	23B (6.1%)	23B (6.6%)	19A (6.6%)	22F (5.7%)	19A (6.0%)	12F (6.0%)

Source: Country reports from Austria, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

** Number of cases for which information on serotype and age was available. Number of cases for which serotype information was available by age group: <1 year: n=390; 1–4 years: n=608; 5–14 years: n= 287; 15–24 years: n=244; 25–44 years: n=1 714; 45–64 years: n=4 218; ≥65 years: n=8 426.*

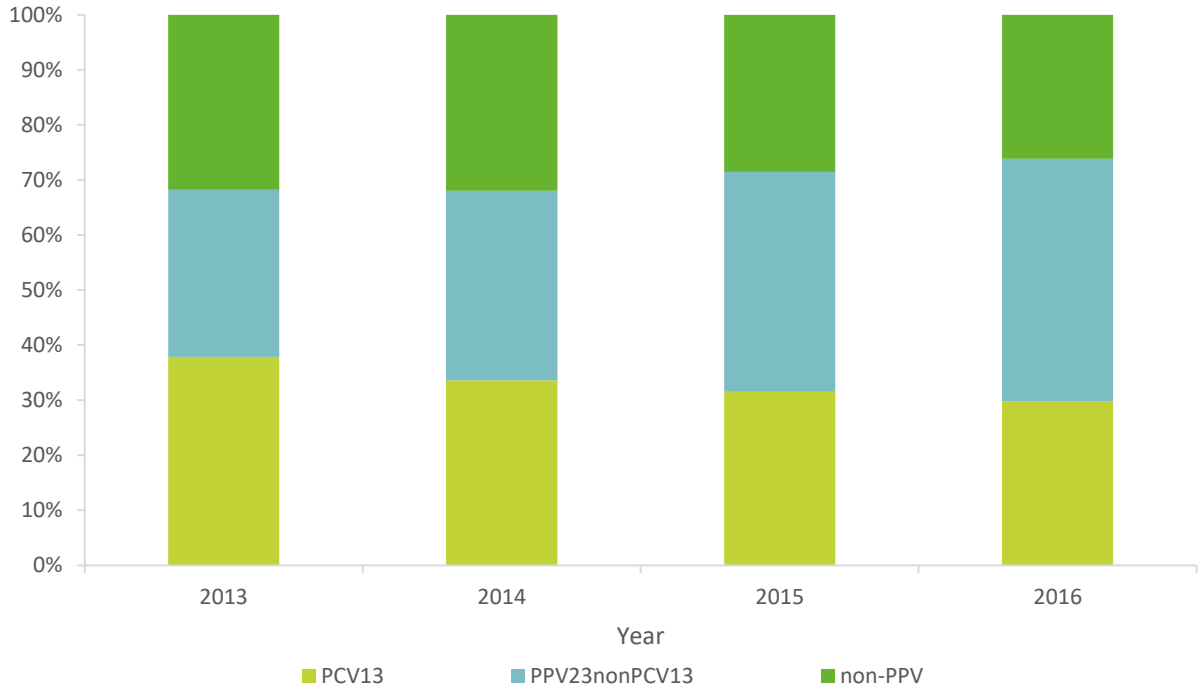
Figure 5. Confirmed cases of invasive pneumococcal disease aged <5 years: serotype distribution by PCV type and year, 2013–2016 (n= 3 712)



** Although serotype 6A is included in PCV13 and not in PCV7, it is considered a PCV7 serotype for the purpose of this analysis due to documented cross-protection provided by serotype 6B antigen in PCV7. PCV7 serotypes: 4, 6A, 6B, 9V, 14, 18C, 19F, 23F; PCV10non7 serotypes: 1, 5, 7F; PCV13non10 serotypes: 3, 19A; non-PCV serotypes: all remaining serotypes.*

Source: Country reports from Austria, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

Figure 6. Confirmed cases of invasive pneumococcal disease aged ≥65 years: serotype distribution by PCV type and year, 2013–2016 (n=29 151)



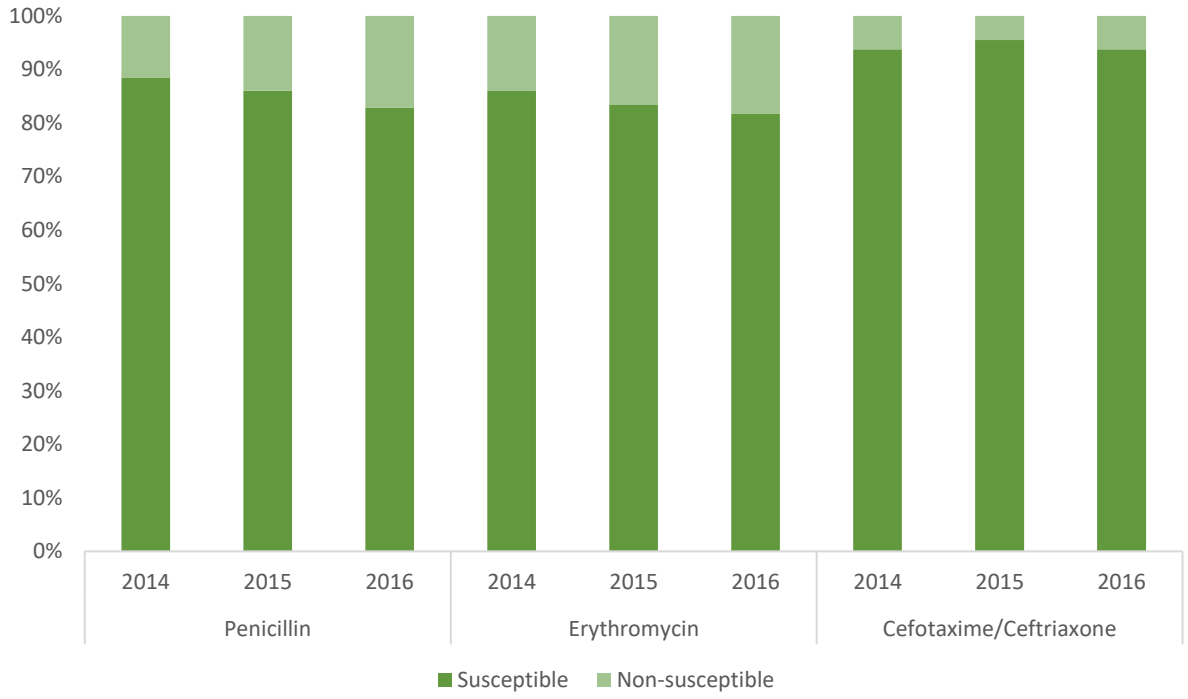
PCV13 serotypes: 4, 6A, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F, 3, 19A; PPV23nonPCV13 serotypes: 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F; Non-PPV serotypes: all remaining serotypes.

Source: Country reports from Austria, the Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

Antimicrobial susceptibility

Data on antimicrobial susceptibility against at least one antimicrobial were reported by 15 countries and for 17 088 (78%) of all cases. In 2016, the prevalence of non-susceptibility (combined intermediate and resistant categories) to penicillin was 17%, to erythromycin 18% and to cefotaxime/ceftriaxone 6%. The highest percentage of non-susceptibility to erythromycin was reported by Hungary (33%), to penicillin by France (25%) and to cefotaxime/ceftriaxone by Spain (12%). From 2014 to 2016, among countries consistently reporting antimicrobial susceptibility data, the prevalence of non-susceptibility increased for penicillin and erythromycin and remained stable for cefotaxime/ceftriaxone (Figure 7).

Figure 7. Susceptibility of *S. pneumoniae* isolates from confirmed cases of invasive pneumococcal disease to penicillin, erythromycin and cefotaxime/ceftriaxone among countries consistently reporting susceptibility data, 2014–2016



Sources: Country reports from Denmark, Estonia, France, Hungary, Iceland, Ireland, Italy, Latvia, Norway, Poland, Slovakia, Slovenia, Spain and the United Kingdom. France and Italy not included for cefotaxime/ceftriaxone.

Total number of penicillin cases in 2014: n=7 418; 2015: n=7 158; 2016: n=6 006
Total number of erythromycin cases in 2014: n=6 739; 2015: n=6 924; 2016: n=6 020
Total number of cefotaxime/ceftriaxone cases in 2014: n=3 907; 2015: n=4 670; 2016: n=3 963.

Note: SIR values (susceptible, intermediate and resistant) as interpreted by the reporting countries. 'Intermediate' and 'resistant' were categorised as 'non-susceptible'.

Clinical presentation

Clinical presentation was known for 7 968 (36%) of all cases. Of these, septicaemia was reported in 2 950 cases (37%), bacteraemic pneumonia in 2 953 (37%), meningitis in 1 745 (22%), meningitis and septicaemia in 105 (1%) and a further 215 cases (3%) had other clinical presentations. The most common clinical presentation in 1-4-year-olds was septicaemia and among < 1-year-olds and 5–14-year-olds, it was meningitis. Among those aged 15 years and over, bacteraemic pneumonia was the most common clinical presentation.

Among the 10 most common serotypes in 2016, 8, 9N, 10A, 11A and 15A were most commonly associated with septicaemia. The other four most common serotypes (3, 19A, 22F and 33F) were most commonly associated with bacteraemic pneumonia, while for serotype 12F, the proportion of septicaemia and bacteraemic pneumonia was similar.

Outcome

Among 10 372 cases with known outcome (47%), 1 800 (17%) were reported as fatal. Three countries (Italy, Poland and the United Kingdom) accounted for 83% of fatal cases.

However, due to low completeness of clinical presentation and outcome data, results must be interpreted with caution and the true case fatality is expected to be considerably lower.

Discussion

The notification rate of 5.4 cases per 100 000 population of confirmed IPD in 2016 was within the range observed between 2012 and 2015 (4.8–5.7 per 100 000). Notification rates varied by country, ranging from 0.2 to 14.9 cases per 100 000 population. The elderly and infants continue to be the most affected age groups. Variation in notification rates between countries may be due to differences in healthcare systems, vaccination programmes, case ascertainment and reporting, and implementation of enhanced surveillance systems in a number of countries in recent years [6].

The overall number of IPD cases has decreased since the introduction of PCV, which has proven effective in reducing the overall number of IPD cases worldwide and in EU/EEA countries [7]. The proportion of cases caused by PCV serotypes decreased across all age groups and the majority of cases in 2016 were caused by non-PCV serotypes. PCV7 was first licensed in 2001 for use in infants and young children and EU/EEA Member States began introducing the vaccine to routine childhood immunisation schedules in 2006. In 2009, higher-valency PCV10 and PCV13 vaccines were licensed and have progressively replaced PCV7. To date, 28 Member States have introduced conjugate vaccines to routine national childhood immunisation programmes [8].

In order to provide further insight into the epidemiology of IPD, ECDC started funding the *Streptococcus pneumoniae* Invasive Disease network (SpIDnet) in August 2012. This project aims to establish active enhanced surveillance of IPD in the EU/EEA in order to monitor changes in the epidemiology of IPD, estimate the effectiveness of PCVs and evaluate the impact of PCV programmes. The project has 12 study sites in 10 Member States and covers around 20% of the total EU/EEA population. The project complements routine surveillance performed in Europe by actively collecting additional data and using a common protocol. A report from August 2017 shows that the incidence of IPD caused by any serotype in children younger than five years decreased by 47% in the PCV10/13 period as compared with the PCV7 period (i.e. before the introduction of PCV10/13) [9]. The decrease is even more substantial (55%) when the period after the introduction of PCV10/13 is compared with the period before the introduction of PCV7. This decline demonstrates the positive overall effect of PCV programmes. By contrast, the incidence of IPD caused by non-PCV13 serotypes in children below the age of five increased by 62% compared with the average incidence when PCV7 was used and 115% compared with the period before PCV7 was used. These results suggest the occurrence of serotype replacement probably due to the use of PCV [10].

A number of other studies have demonstrated the effectiveness of PCVs in reducing the incidence of IPD. They also provide evidence of increases in non-vaccine serotypes as an effect of the introduction of PCV10 and PCV13 [11-13]. Moreover, the vaccination of infants and young children has resulted in indirect protection of older adults by reducing nasopharyngeal carriage and transmission of the bacterium, contributing to a decrease in morbidity and mortality in older age groups [11,14]. Over time, serotype replacement has gradually reduced the effectiveness of PCV7 as the rates of carriage and disease caused by non-vaccine serotypes have increased [15]. In the IPD cases reported to ECDC in 2016 among infants and children aged 1–4 years, the most common serotypes included 8, 10A, 12F and 24F, which are not included in any of the currently licensed PCVs. These serotypes could be potential targets for future higher-valency vaccines.

Among the elderly, the majority of IPD cases continue to be caused by PPV23 serotypes, with a third of all cases caused by PCV13 serotypes. In 2011, PCV13 was approved for use in adults aged 50 years and over. Studies have shown that PCV13 vaccination in the elderly can induce an immune response against vaccine serotypes that is as good as or better than PPV23 [16]. The vaccine is safe and effective in preventing non-invasive pneumococcal pneumonia and IPD [16]. However, decreases in PCV13 serotypes and increases in non-PCV13 serotypes in the elderly as an indirect effect of routine childhood vaccination may decrease the potential additional benefit of PCV13 vaccination in the elderly [17]. Further monitoring of IPD serotype trends in the elderly and post-marketing impact studies in adults are warranted. Twenty-one Member States offer different vaccines for persons 50 years of age and over and/or for risk groups in certain age groups. Fifteen Member States offer PPV23 and 10 offer PCV13 vaccination for the elderly [8].

From 2014 to 2016, the prevalence of non-susceptibility of *Streptococcus pneumoniae* increased for penicillin and erythromycin and remained stable for cefotaxime/ceftriaxone. According to a recent study, an increase in non-vaccine serotype non-susceptibility to penicillin and erythromycin was observed in children under five years of age [18]. Continued long-term monitoring of antimicrobial non-susceptibility is crucial to detect the emergence of non-vaccine non-susceptible serotypes.

Public health implications

PCVs have provided significant protection against IPD due to vaccine serotypes, with effects extending to all age groups through the introduction of herd immunity. At the same time, the limited serotype coverage of the vaccines have allowed serotype replacement. It is therefore essential to continue to monitor circulating serotypes in order to evaluate current vaccination programmes and inform the development of new vaccines. The decision to introduce a vaccine to a routine national immunisation programme depends on context-specific factors in each country such as disease burden, serotype distribution and cost effectiveness. Further monitoring of antimicrobial resistance is necessary in order to guide treatment options.

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